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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,112	HEYMAN ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *34* is/are withdrawn from consideration.

5)☒ Claim(s) *32 and 33* is/are allowed.

6)☒ Claim(s) *1-7 and 12-31* is/are rejected.

7)☐ Claim(s) *8-11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,12,13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group 1-33 in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Specification

2. The use of the trademark "Zeocin" at page 12 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 4 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 4 is indefinite for the recitation of abbreviations, e.g., nCBP, because abbreviations often have more than one meaning in the art. It is suggested reciting the full name of the abbreviations in the claim.

(b) Claim 10 is indefinite for the recitation of "capable of" because it cannot be clearly determined if the limitation after "capable of" is property of the site-specific recombinase or a separate method step. It is suggested changing "capable of recognizing" to "which recognize" or some other active language as supported by the specification as originally filed.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 12, 13, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Scheele (US 5,162,209, November 10, 1992). Regarding claim 1, Scheele teaches a method of producing a full-length coding sequence, said method comprising: synthesizing first strand cDNA using isolated full length mRNA from a population of cells as a template, thereby forming first strand cDNA/mRNA hybrids(s); denaturing the first strand cDNA/mRNA hybrids(s); attaching a non-native tag sequence to the 3' end of the first strand cDNA; and producing a full length double stranded cDNA by synthesizing second strand cDNA using the tagged first strand cDNA produced in the previous step (col. 3, line 60 to col. 5, line 41).

Regarding claim 12, Scheele teaches the method of claim 1 further comprising amplifying the cDNA after the producing step (col. 8, lines 58-61).

Regarding claim 13, Scheele et al. teach the method according to claim 12, further comprising inserting the full-length cDNA into an expression vector (col. col. 3, line 65 to col. 4, line 2).

Regarding claims 20 and 21, Scheele teaches an isolated full length coding sequence prepared according to the method of claim 1 and a expression vector comprising an isolated full-length coding sequence prepared according to the method of claim 1 (col. 3, line 63 to col. 4, line 2). Therefore, the Scheele meets the limitations of claims 1, 12, 13, 20 and 21 of the instant invention.

7. Claims 1, 12, 13, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Chenchik et al. (W) 97/24455, July 10, 1997). Regarding claim 1, Scheele teaches a method of producing a full-length coding sequence, said method comprising: synthesizing first strand cDNA using isolated full length mRNA from a population of cells as a template, thereby forming first strand cDNA/mRNA hybrids(s); denaturing the first strand cDNA/mRNA hybrids(s); attaching a non-native tag sequence to the 3' end of the first strand cDNA; and producing a full length double stranded cDNA by synthesizing second strand cDNA using the tagged first strand cDNA produced in the previous step (Abstract and page 3, line 29 to page 5, line 35).

Regarding claim 12, Scheele teaches the method of claim 1 further comprising amplifying the cDNA after the producing step (page 13, lines 13- 36).

Regarding claim 13, Scheele et al. teach the method according to claim 12, further comprising inserting the full-length cDNA into an expression vector (page 14, lines 1-15).

Regarding claims 20 and 21, Scheele teaches an isolated full length coding sequence prepared according to the method of claim 1 and a expression vector comprising an isolated full-length coding sequence prepared according to the method of claim 1 (pages 4-14). Therefore, Chenchik et al the meets the limitations of claims 1, 12, 13, 20 and 21 of the instant invention.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik et al. as previously applied in view of Edery (Molecular and Cellular Biology, Vol. 15, No. 6, pages 3363-3371, June 1995). Regarding claim 4, Chenchik et al teaches a method of producing a full-length coding sequence, said method comprising: synthesizing first strand cDNA using isolated full length mRNA from a population of cells as a template, thereby forming first strand cDNA/mRNA hybrids(s); denaturing the first strand cDNA/mRNA hybrids(s); attaching a non-native tag sequence to the 3' end of the first strand cDNA; and producing a full length double stranded cDNA by synthesizing second strand cDNA using the tagged first strand cDNA produced in the previous step. Chenchik differs from the instant invention in that Chenchik does not teach wherein an affinity purification material comprising one or more cap binding proteins wherein the cap binding protein is are selected from the group consisting of eIF4E, eIF4F, eIF4G, nCBP and eIF4E:eIF4G fusion protein. Edery et al. teach a method for producing a full-length cDNA based on an affinity selection procedure using a fusion protein contain the murine cap-binding protein (eukaryotic initiation factor E4) coupled to a solid support matrix, that allows for the purification of MRNAs via the 5' cap structure. The reference teaches when combined with a RNA digestion step, specific retention of complete/RNA duplexes following first strand synthesis is achieved (see abstract). Edery et al teaches that the use of the cap binding protein, eukaryotic initiation factor E4 is advantageous because this protein shows string binding specificity for methylated cap structures of eukaryotic mRNAs (pages 3363, col. 2, first full paragraph). Therefore, in view of the foregoing, one of ordinary skill in the art would have been motivated to provide a cap-binding protein such as eIF4E to the method of Chenchik

because of the advantages taught by Edery that cap-binding proteins such as eIF4E have strong binding specificity.

11. Claims 2, 3, 5, 6, 7,13-19, 21 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik as previously applied above in view of Carninci et al. (Genomics, Vol. 37, No. 3, pages 327-336, 1996). Regarding claims 2, 3 and 5, Chenchik teaches a method of producing a full-length coding sequence, said method comprising: synthesizing first strand cDNA using isolated full length mRNA from a population of cells as a template, thereby forming first strand cDNA/mRNA hybrids(s); denaturing the first strand cDNA/mRNA hybrids(s); attaching a non-native tag sequence to the 3' end of the first strand cDNA; and producing a full length double stranded cDNA by synthesizing second strand cDNA using the tagged first strand cDNA produced in the previous step. The method of Chenchik differs from the instant invention in that the reference does not expressly teach isolation of the mRNA or wherein the mRNA to be isolated comprises a biotinylated cap structure and the affinity purification material comprises one or more cap binding proteins bound to a solid support. Carninci et al teach a method similar to that of Chenchik for producing a full length cDNA molecule, the method comprising: synthesizing a first strand cDNA using isolated full-length mRNA which comprises a biotinylated cap structure, thereby forming a first strand cDNA/mRNA hybrids; denaturing the first strand hybrids and recovering full length double stranded cDNA after RNase I treatment (See entire section entitle "Results" pages 329, column 2 to page 3, column 1, first-fourth paragraphs). Carninci et al. additionally teach wherein the mRNA is isolated employing an affinity purification material comprising one or more cap-binding proteins bound to a solid surface (Abstract). Carninci et al further teach capping the mRNA using a cap-binding structure

useful because it selects only for full-length cDNA (Abstract). Therefore in view of the foregoing, one of ordinary skill in the art would have been motivated to have modified the method of Chenchik to incorporate a cap-binding structure in the method of producing a full length cDNA as taught by Chenchik for the benefit of specifically selecting only for full-length cDNA as taught by Carninci et al.

Regarding claim 6, Carninci et al. teach wherein the affinity purification material is a streptavidin-complex solid support (page 329, col. 2, section entitled "Biotinylation of Diol Groups of RNA").

Regarding claims 13, Carninci et al. teach wherein the method further comprises inserting the cDNA into an expression vector (page 331, section entitled "Second-strand cDNA synthesis and Cloning" and "Full-length cDNA representation of GAPDH and EF-1-α").

Regarding claims 14 and 15, Carninci et al. teach wherein the method comprises treating the first strand cDNA/mRNA hybrids formed in step (a) with a substance that degrades single stranded RNA; and isolating the under-graded hybrid(s) with an affinity purification material having affinity for capped mRNA prior to performing step (b), wherein said substance is RNase I (see abstract and Figure 1).

Regarding claim 16-18, Carninci et al. teach wherein the mRNA component of the cDNA/mRNA hybrid comprises a biotinylated cap structure and wherein the affinity purification material is a streptavidin complex solid support (page 329, col. 2, section entitled "Biotinylation of Diol Groups of RNA" and abstract).

Regarding claims 21, Carninci et al. teach an expression vector, (Lambda Zap II expression vector) comprising an isolated full-length coding sequence prepared according to the

method of claim 1 (page 331, sections entitled "Second-strand cDNA synthesis and Cloning" and "Full-length cDNA representation of GAPDH and EF-1-α").

Regarding claim 30, Carninci et al teach wherein the expression vector is Lambda Zap II expression vector (page 331, section entitled "Full-length cDNA representation of GAPDH and EF-1-α"). Lambda Zap II expression vector id a prokaryotic expression vector. Therefore, the limitation of this claim is inherent in the teaching of the vector by name.

12. Claims 21-24, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik and Carninci et al. as previously applied and further in view of Sambrook et al. (Molecular Cloning, A laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989). Regarding claim 21-24, 30, Chenchik and Carninci et al. teach an expression vector comprising an isolated full-length coding sequence prepared according to the method of claim 1. Carninci et al further teach wherein the expression vector is a bacteriophage lambda Zap II expression vector. The references do not expressly teach the elements of the expression vector. However, the elements of the lambda Zap II vector is taught in general laboratory manual by Sambrook et al. Sambrook et al disclose the characteristics of the lambda Zap II vector and elements that the vector comprises therein. These include a T7 promoter-enhancer, a selection marker encoding a protein which imparts antibiotic resistance to cells and an origin of replication (see pages 2.53 and 2.54). Sambrook et al teach that the vector is useful because expression of fusion proteins and production of capped RNA transcripts are readily obtainable (page 2.53, first paragraph). Therefore in view of the foregoing, one of ordinary skill in the art would have been motivated to utilize a Lambda Zap II expression vector comprising the isolated full-length coding sequence prepared by the method of claim 1 for the advantages taught by

Sambrook that the Zap II vector is useful because expression of fusion proteins and production of capped RNA transcripts can be readily obtainable.

Regarding claim 31, Sambrook et al. teach an expression vector according to claim 30, wherein the eukaryotic expression vector is pMT expression vector (see 16.20 last paragraph and 16.22, entire page).

13. Claims 26 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik and Carninci et al as previously applied and further in view of Jacobs, Jr. et al (US 5,981,182, filing date March 13, 1997). Regarding claim 29, Chenchik and Carninci et al. teach an expression vector comprising an isolated full-length coding sequence prepared according to the method of claim 1. Carninci et al further teach wherein the expression vector is a bacteriophage lambda Zap II expression vector. The references do not expressly teach wherein the vector comprises a polypeptide encoding sequence which includes an intein encoding sequence. Jacobs, Jr et al teach vector constructs for the selection and identification of open reading frames. Jacobs. Jr et al teach wherein the vectors may comprise a pBluescript II or lambda Zap II vector (col. 7, lines 12-18) and wherein the vector may comprise a polypeptide encoding sequence which includes an intein encoding sequence (col. 5, lines 17-23). Jacobs, Jr. et al further teach that an intein is a protein sequence which, during protein splicing, is excised from a protein precursor (col. 5, line 17-20). The reference further teaches that vectors constructs comprising inteins are unique in that that they utilized the protein splicing properties of the inteins which is useful for the identification of potentially protective antigens of a pathogen (col. 10, lines 42-65). Therefore, in view of the foregoing, one of ordinary skill in the art would have been motivated to provide an expression vector as taught by Chenchik in view of

Carninci et al that comprises an intein encoding sequence for the unique protein splicing properties of inteins as taught by Jacobs, Jr. et al.

14. Claims 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik and Carninci et al. as previously applied and further in view of Elledge et al. (US 5,851,808, December 22, 1998). Regarding claims 26-28, Chenchik and Carninci et al. teach an expression vector comprising an isolated full-length coding sequence prepared according to the method of claim 1. Carninci et al further teach wherein the expression vector is a bacteriophage lambda Zap II expression vector which is capable of expressing fusion proteins. The references do not teach wherein the expression vector comprises a glutathione-S-transferase polypeptide or a polyhistidine tract. In a general reference, Elledge et al teach rapid subcloning using site-specific recombination. Elledge et al teach an expression vector (pHOST vector) which have been modified by the insertion of a sequence-specific recombinase target site. The reference further teaches wherein the vector may encode a protein domain such as an affinity domain including, but not limited to, glutathione-S-transferase, a polyhistidine tract and etc. (col. 16, lines 50-62). The reference teaches that the vector is useful because it permits the rapid exchange of an entire cDNA library to a variety of expression vectors (col. 18, lines 38-42). Therefore, in view of the foregoing, one of ordinary skill in the art would have been motivated to have modified the expression vector of Chenchik et al. and Carninci et al to incorporate a glutathione-S-transferase polypeptide and a polyhistidine tract as taught by Elledge et al for the benefits of providing an expression vector which permits the rapid exchange of an entire cDNA library to a variety of expression vectors as suggested by Elledge et al.

Conclusion

15. Claims 1-7, 12-31 are rejected. Claims 8-11 and 32-33 are free of the prior art. Claims 8-11 are objected because they depend from a rejected claim. The claims 8-11 and 32-33 are free of the prior art because the prior art does not teach a method of obtaining a full-length coding sequence comprising attaching a non-native tag sequence to the single stranded cDNA isolated in the previous steps (a) through (d), wherein the tag sequence comprises a site specific recombination sequence and is attach by *E. coli* topoisomerase III and synthesizing second strand cDNA using the tagged cDNA as a template and/or amplifying the cDNA, wherein the amplification primers comprises an anti-coding sequence of the tag sequence (5') and oligo-dT(3').

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308 0196.

CYNTHIA WILDER
PATENT EXAMINER

Cynthia B. Wilder, Ph.D.
Examiner
Art Unit 1637

cbw
September 9, 2003